Mechanistic Investigations on the Reaction between 1,2-Dioxines and Bulky Stabilized Phosphorus Ylides: An Efficient Route to Closely Related Cyclopropane Stereoisomers

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The bulky stabilized ylides (**2a**−**d**) react with a range of 1,2-dioxines (**1a**−**d**) to afford the diversely functionalized cyclopropanes **7** in excellent yield and diastereomeric excess. This is in direct contrast to the situation when nonbulky ester ylides are utilized which results in a completely different cyclopropyl series. Through a combination of isolation, spectroscopic, temperature, and deuterium and additive effects studies, the mechanism of cyclopropane formation from this second pathway can be proposed. Importantly, enolate quenching of the intermediate 1-2λ^5-oxaphospholanes **4** prior to collapse results in an equilibrium mixture of intermediates **10** and **11** which have been fully characterized, and their formation is primarily a result of the steric bulk of the stabilized ester ylide. These intermediates (**10**/**11**) then collapse further and result in formation of the observed closely related cyclopropyl stereoisomers **7** and **8**. Moreover, the addition of LiBr to these reactions allows for the control of which of the two possible cyclopropanation pathways will be dominant. Finally, optimal protocols that demonstrate the potential of this new cyclopropanation methodology for the ready construction of closely related cyclopropyl stereoisomers are presented.

Introduction

Functionalized cyclopropanes have proven to be exceedingly useful building blocks for the synthesis of natural and nonnatural products.[1] Although there exists many excellent ways for the construction of the cyclopropyl core,[2,3] the great importance of functionalized cyclopropanes in organic synthesis spurs a continuing search for efficient stereocontrolled cyclopropanation methodologies. Of particular importance is the deficiency in methods for the construction of diversely functionalized cyclopropanes that contain greater than disubstitution.

Our efforts have focused on exploiting 1,2-dioxines **1** and stabilized phosphorus ylides **2** (e.g. R^1 = Me, Et, Bn, etc.) as precursors for the construction of diversely functionalized cyclopropanes **5**. We have recently reported on the mechanism and scope of reaction when nonbulky ester stabilized phosphorus ylides are utilized.[4] Key features of this cyclopropanation, Scheme 1 pathway a, include the ylide acting as a mild base inducing the ring opening of the 1,2-dioxines **1** to their isomeric cis γ-hydroxy enones **3**, followed by Michael addition of the ylide to the enone and attachment of the electrophilic phosphorus pole of the ylide to the hydroxyl moiety affording the intermediate 1-2λ^5-oxaphospholanes **4** and setting up the observed cis stereochemistry between H1 and H3. Cyclization of the resultant enolate, expulsion of triphenylphosphine oxide followed by proton transfer affords the observed cyclopropanes **5** in excellent yield and diastereomeric excess.[4] This cyclopropanation pathway a provides for a range of substituents (X, Y = H, alkyl or aryl) at the 3- and 6-positions of the 1,2-dioxine

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(2) For examples of the direct carbene transfer (both stoichiometric and catalytic) from a diazo precursor to an olefin utilizing transition metals see: Denmark, S. E.; Christenson, B. L.; O'Conner, S. P.; Murase, N. *Pure Applied Chem.* **1996**, *68*, 23. Boverie, S.; Simal, F.; Demonceau, A.; Noels, A. F.; Eremenko, I. L.; Sidorov, A. A.; Nefedov, S. E. *Tetrahedron Lett.* **1997**, *38*, 7543. Demonceau, A.; Simal, F.; Noels, A. F.; Viñas, C.; Nunez, R.; Teixidor, F. *Tetrahedron Lett.* **1997**, *38*, 7879. Singh, V. K.; DattaGupta, A.; Sekar, G. *Synthesis*, **1997**, 137. Ichiyanagi, T.; Shimizu, M.; Fujisawa, T. *Tetrahedron*, **1997**, *53*, 9599. Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 971. Davies, H. M. L.; Panaro, S. A. *Tetrahedron Lett.* **1999**, *40*, 5287.

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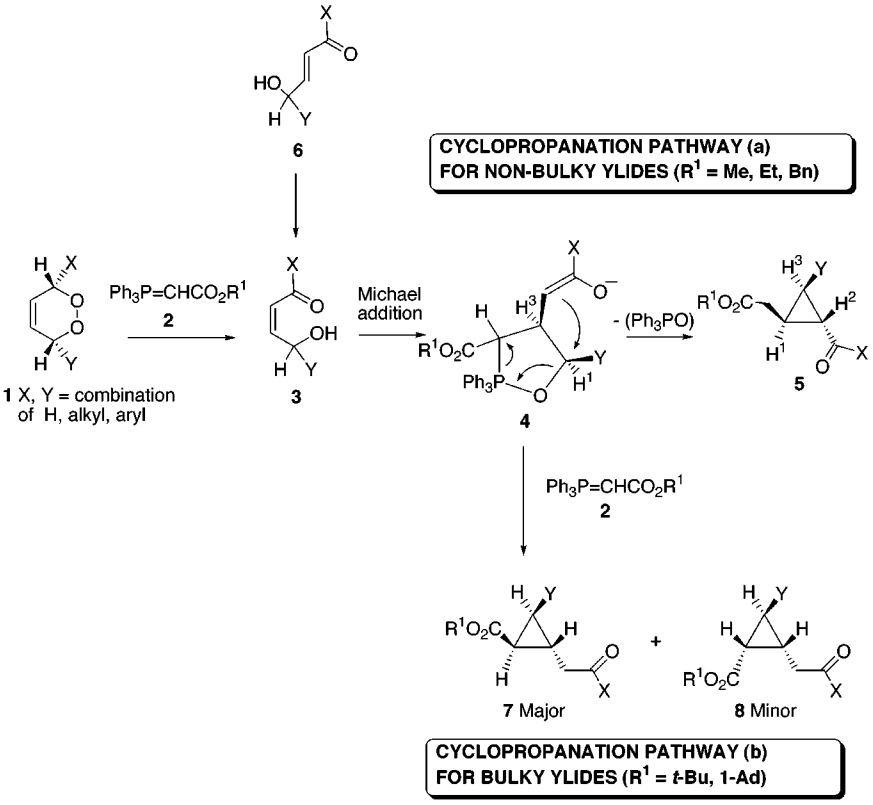
Scheme 1



1 which accommodates for the synthesis of both di- and trisubstituted cyclopropanes. In addition, this cyclopropanation pathway may be entered utilizing the related trans γ-hydroxy enones **6**, which, if optically pure, allows for the synthesis of enantiopure cyclopropanes **5**.[5]

Further to these findings we have recently communicated that utilization of bulky ester stabilized ylides (e.g., **2**, R^1 = *t*-Bu) favors the formation of a completely different diastereomeric cyclopropyl series, Scheme 1, pathway b.[6] For example, treatment of 1,2-dioxine **1a** (X = Y = Ph) with the *tert*-butyl ester stabilized ylide at −15 °C led to the formation of cyclopropanes **7** and **8** as the sole products in a relative ratio of 91:9, respectively. Preliminary mechanistic studies also revealed that the use of sterically bulky ester ylides under concentrated conditions favored the first cyclopropanation pathway (i.e., formation of **5**) while dilute conditions favored the formation of cyclopropanes **7** and **8**. Furthermore, subambient temperatures were found to favor the second cyclopropanation pathway b.

This contribution reports on detailed mechanistic studies, which have allowed a mechanistic rationale behind the second cyclopropanation pathway b to be proposed. Furthermore, optimization of several of the key experimental parameters has allowed the overall synthetic utility of these cyclopropanation manifolds to be extended greatly.

Results and Discussion

Elucidation of Key Intermediates. Although the second cyclopropanation pathway can accommodate for the utilization of a diverse range of 1,2-dioxines (e.g., X, Y = H, alkyl or aryl) and bulky ester stabilized ylides (e.g., *t*-Bu, 1-adamantyl) (see Table 2) we have essentially utilized only the symmetrical 1,2-dioxine **1a** (X, Y = Ph) for the mechanistic studies. Thus, monitoring the reaction between 1,2-dioxine **1a** with the *tert*-butyl ester ylide **2** (R^1 = *t*-Bu) by ^{31}P NMR at 25 °C revealed the initial formation of two phosphorus containing intermediates corresponding to signals at δ 23.99 and δ 24.29 ppm. These two intermediates (**10** and **11**) which were in a relative ratio ca. 9:1, respectively, then decayed over 12 h to afford the observed cyclopropanes **7**, **8** (X = Y = Ph, R^1 = *t*-Bu) and TPPO. This is in stark contrast to cyclopropanation pathway a in which no phosphorus containing intermediates could be detected.[4] These chemical shifts are inconsistent with a neutral pentavalent oxaphospholane ring of type **4** and are more appropriately assigned as being due to charged species with ylide characteristics. For comparison, the phosphorus atom within the 1-2λ^5-oxaphospholane ring system is expected to exhibit a ^{31}P NMR resonance in the δ −40 to −60 ppm range[7,8] while that for the *tert*-butyl 2-(triphenyl-λ^5-phosphanylidene) acetate ylide appears at +17.2 ppm. Moreover, it was clearly evident that formation of intermediate **10** preceded the formation of intermediate **11**. This observation was conclusively confirmed when the same reaction was monitored by ^{1}H NMR. Two intermediates were clearly observable with the formation of **11** lagging behind formation of **10**. The ratios of these two intermediates stayed essentially constant as they decayed with concomitant cyclopropane formation. Cyclopropanes

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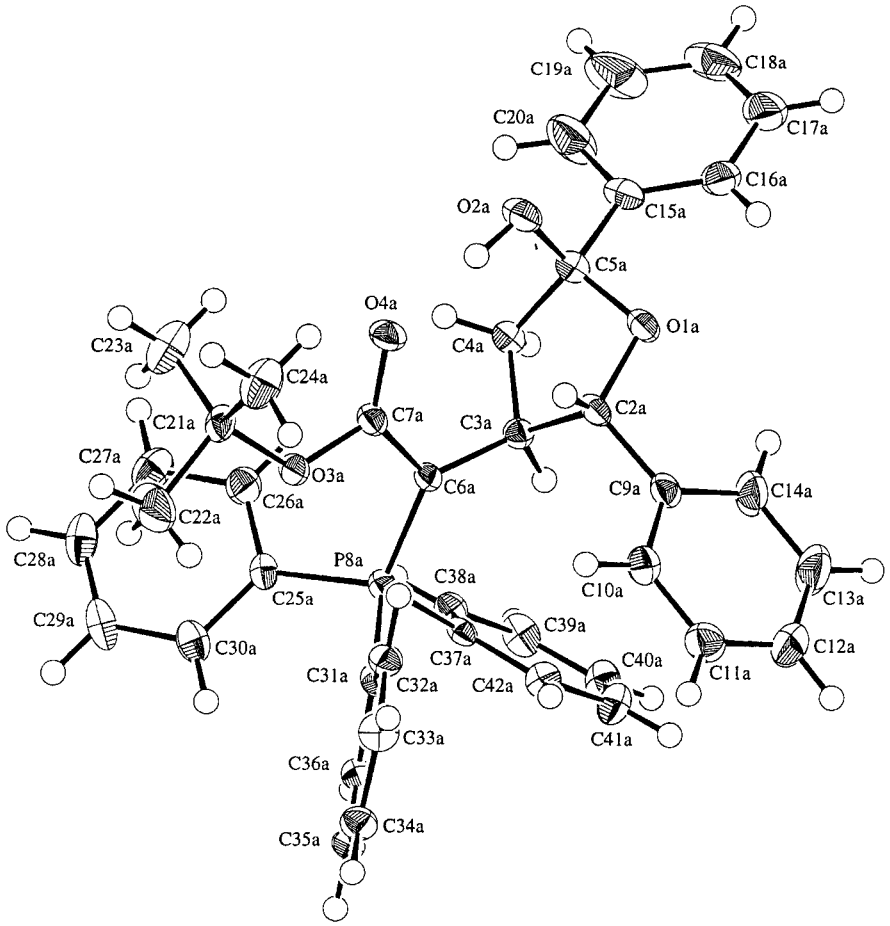

Figure 1. Molecular structure of one of the two independent molecules in **11**.

from both possible pathways were formed in this experiment in a relative ratio of **5** (19):**7** (70):**8** (8). Of particular importance was the observation that formation of **5** was extremely facile and ceased when all the 1,2-dioxine had been consumed, however, formation of **7** and **8** relied on the formation of intermediates **10** and **11**.

Exploiting the facile $Co(SALEN)_2$ catalyzed isomerization of the 1,2-dioxine **1a** into the cis γ-hydroxy enones **3**,[4,6] allowed us to generate **10** and **11** at lower temperature. Thus, treatment of **1a** with a catalytic amount of $Co(SALEN)_2$ in $CDCl_3$ followed by the addition of the *tert*-butyl ylide (1 equiv) and storage at −15 °C for 2 days allowed for the formation of only **10** and **11** without any further decomposition to cyclopropanes. None of cyclopropane **5** was formed at this subambient temperature while allowing the mixture to attain ambient temperature led to the formation of cyclopropanes **7** and **8** as the sole products in a relative ratio of 91:9, respectively. To try to influence the relative ratio of **10**/**11**, we prepared **10**/**11** in a range of deuterated solvents ($CDCl_3$, acetone-d_6, C_6D_6, DMSO-d_6 and CD_3CN), however, we found that the ratio remained essentially constant. Importantly, the use of deuterated acetonitrile led to the formation of crystals when the mixture was allowed to attain ambient temperature. Isolation and dissolution in $CDCl_3$ revealed these crystals to be pure **11**. Moreover, monitoring by ^1H NMR revealed that **11** reequilibrates at ambient temperature to reform a 7:3 mixture of **10** and **11**, respectively, confirming that **11** originates from **10**. This equilibrium was found to take 8 days to reestablish at −15 °C without any appreciable decomposition to cyclopropanes **7** and **8**. Warming to ambient temperature again led to cyclopropanes **7** and **8** and TPPO in a 86:14 cyclopropyl ratio. It was found that **11** was indefinitely stable if kept in the crystalline state at ambient temperature. The structure of **11** was fully established by single-crystal X-ray diffraction methods and is depicted in Figure 1. Ylide **11** represents the first reported example of a crystalline stabilized phosphorus ylide containing a hemiacetal moiety.

Key features of the NMR spectra of **11** include the ylide type phosphorus (δ_P 24.29 ppm), the ester carbonyl (δ_C 169.90 ppm), and the hemiacetal carbon (δ_C 104.6 ppm). In comparison, inspection of the NMR spectra of the equilibrium mixture of **10**/**11** allowed the structure of **10** to be established. **10** contained an ylide type phosphorus (δ_P 23.99 ppm), an ester carbonyl (δ_C 172.5 ppm), a ketone carbonyl (δ_C 203.3 ppm), but no hemiacetal carbon thus indicating that **10** was not the trans isomer of the hemiacetal **11**. This together with the COSY spectrum, which showed essentially the same spin system as found in **11**, indicated that **10** was the open chain phosphanylidene pentanoate **10**, Scheme 2. This structure was confirmed by examination of the HMBC spectrum.

Proposed Mechanism for the Second Cyclopropanation Pathway b. With the structure of both intermediates now established, a mechanism for the formation of cyclopropanes **7** and **8** and the subtle difference between this and the first cyclopropanation pathway a can be presented. Thus, for both bulky and nonbulky ylides, the ylide acts as a mild base inducing ring opening of the 1,2-dioxine **1** into the isomeric cis

Table 1. Deuterium Labeling Studies When X, Y = Ph and R^1 = *t*-Bu[a]

entry	starting material	reaction time[b]	products[c]
1	**1**	4 weeks	1′-CD_2-**5**; 77% 1′-CHD-D^4-**7**: 17%; 1′-CHD-D^4-**8**; 6%
2	**3**	5 days	As for entry 1
3	**10** and **11**	5 days	D^4-**7**: 80%; D^4-**8**; 20%
4[d]	**3**	5 days	**5**; 2%; **7**; 86%; **8**; 12%
5[e]	**3**	4 days	**5**; 42%; **7**; 57%; **8**; 1%

[a] All reactions performed under identical reaction volumes and concentrations at ambient temperature in CH_2Cl_2 as solvent (25 mL) with D_2O (1 mL) present. Starting material (200 mg) utilized for each experiment. Ylide (1.3 equiv) utilized for all experiments except entry 3. Cis γ-hydroxy enone **3** generated by the Co(S-ALEN)$_2$-catalyzed isomerization of the 1,2-dioxine **1a**, see ref 4. [b] Total reaction time necessary for complete consumption of starting material. [c] Ratio of products determined by ^{1}H NMR after cessation of reaction. All reactions resulted in 100% conversion of the starting material into cyclopropanes. Percentage of deuterium incorporation >99% in each case. 1′-CD_2 and 1′-CHD reflect deuterium incorporation with the sidearm while D^4 reflects deuterium incorporation at H^4 of **7**/**8**, see Scheme 2. [d] No D_2O added. [e] H_2O (1 mL) added.

γ-hydroxy enone **3**. Syn Michael addition leads to the intermediate 1-2λ^5-oxaphospholane **4** and sets up the observed cis stereochemistry between H1 and H3. The competition between the first cyclopropanation pathway a and the second cyclopropanation pathway b results from the conformational influence that the R^1 ester moiety has on the conformation of the 1-2λ^5-oxaphospholane enolate **4**. Thus, for nonbulky R^1 substituents (e.g., Me, Bn) the nucleophilic carbon pole of the enolate is favorably aligned for intramolecular S_N2 displacement of TPPO resulting in cyclopropane **5** formation, pathway a. Conversely, the increased steric bulk of bulky R^1 substituents (e.g., *t*-Bu, 1-Ad) results in a diminished alignment for intramolecular S_N2 and actually favors intramolecular proton quenching of the enolate by removal of the proton attached to the 1-2λ^5-oxaphospholane ring oxygen leading to the neutral 1-2λ^5-oxaphospholane **9**. This rationale provides a possible explanation for the observed preference of cyclopropane **7**/**8** formation over **5** in the aforementioned experiments. Furthermore, this rationale is also consistent with our previous observations that elevated temperatures favor the first cyclopropanation pathway a,[6] i.e., elevated temperatures disrupt the preferred minimal conformational preference of **4** when R^1 is bulky and favor intramolecular S_N2 displacement.

At subambient temperatures scission of the P−O bond and proton transfer within the 1-2λ^5-oxaphospholane **9** leads to observed **10** which can exist in equilibrium with the isomeric hemiacetal **11**. Ring openings of oxaphospholanes to afford nonstabilized ylides of a type similar to that of **10** have been noted previously.[7,9] At ambient temperatures and above, **10** and **11** can revert back to the oxaphospholane **9** which undergoes C−P bond fission leading to zwitterionic **12**. An example of this type of ring opening has been postulated previously during the reaction of styrene epoxide with the ethyl 2-(triphenyl-λ^5-phosphanylidene) acetate ylide.[10] At this point intermediate enolates **13a** and **13b** can undergo intramolecular cyclization to afford the observed cyclopropanes **7** and **8**, respectively, and TPPO. Steric buttressing between the bulk of the enolate and the $CH_2C(O)X$ sidearm disfavors cyclopropane **8** formation at nonelevated temperature.

Given that the proposed mechanism[11] requires a number of key proton movements we decided to further probe the validity of the mechanism with a series of deuterium labeling studies, the results of which are summarized in Table 1, while the "expected" positions for deuterium incorporation are superimposed in Scheme 2. Examination of the data within Table 1 (entries 1 and 2) reveals that cyclopropane **5** formation via pathway a results in two deuteriums being incorporated within the sidearm. This result is independent of whether the manifold is entered via the 1,2-dioxine **1** or from the cis γ-hydroxy enone **3**. The incorporation of a single deuterium within the sidearm of cyclopropane **5** is accounted for by the known fact that stabilized phosphorus ylides in the presence of D_2O are expected to readily undergo H−D exchange.[12] The incorporation of the second deuterium is consistent with our previously proposed mechanism in which cyclization of the enolate anion within **4**, TPPO expulsion, and proton (deuteron) "pickup" from the reaction manifold affords the observed cyclopropanes **5**.[4] The incorporation of deuterium at position (H^4) within cyclopropanes **7** and **8** is also consistent with the known rapid H−D exchange for stabilized phosphorus ylides, entries 1,2.[12] Importantly, the incorporation of a single deuterium within the $CH_2C(O)X$ sidearm of **7**/**8** is accounted for by the proposed quenching of the enolate **4**, pathway b. Submitting pure undeuterated cyclopropanes **5**, **7**, or **8** back into the same reactions fails to lead to any deuterium incorporation, indicating that deuterons are incorporated prior to cyclopropane formation.

Exposure of pure **11** to D_2O also allows for rapid (OH) → (OD) exchange. Tracing this scenario through the

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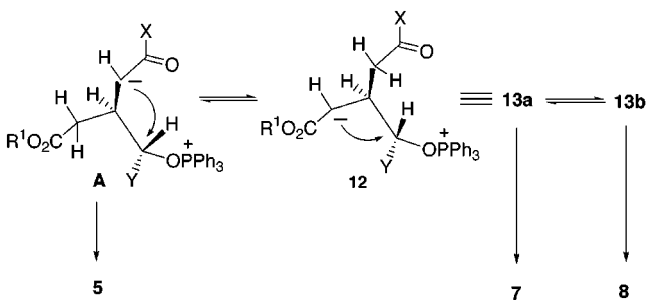
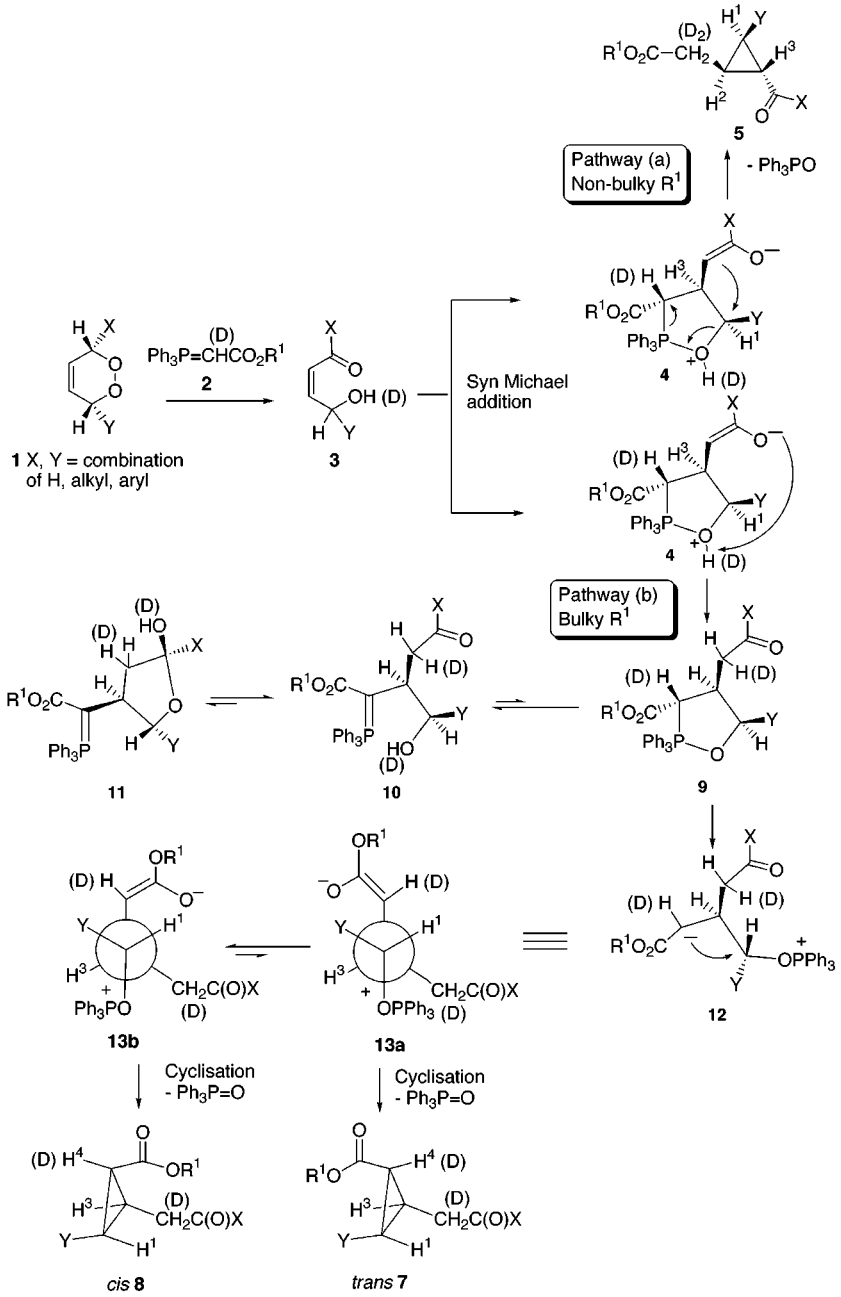
(11) A referee has suggested an alternative mechanistic rationale for cyclopropane formation which avoids the closure to oxaphospholane **4**. Their interpretation is essentially focused on the fact that equilibration (proton transfer) between ester enolate **12** (Scheme 2) and the corresponding ketone enolate (**A**, shown below) normally would thermodynamically favor the ketone enolate **A** for an unhindered ester, irrespective of which enolate (**A** or **12**) is generated first; subsequent intramolecular displacement of TPPO would be fast. Collapse of **A** would lead to cyclopropanes of type **5** when R^1 is unhindered, while collapse through **13a**/**13b** would afford **7**/**8** when R^1 is bulky. The role of LiBr in promoting formation of **7** and **8** would be due to the coordination of the Lewis basic ester with the Lewis acid with consequent enhancement of the steric effect. Given that there are a large number of proton transfers in operation for the competing cyclopropanation processes and that these will be affected in different ways by temperature, concentration, and addition of additives such as LiBr or H_2O/D_2O, it is conceivable at this stage that providing there is a direct route to either **12** or **A** from ylide and **3** then the above alternative mechanistic rationale is plausible. At this stage, however, we have no evidence to suggest that the ketone or ester enolates can be formed without the intermediacy of oxaphospholane **4**.



(12) Labuschagne, A. J. H.; Schneider, D. F. *Tetrahedron Lett*. **1983**, *24*, 743. Hon, Y.-S.; Sheu, T.-R.; Lee, C.-F. *Synth. Commun*. **2000**, *30*, 97.

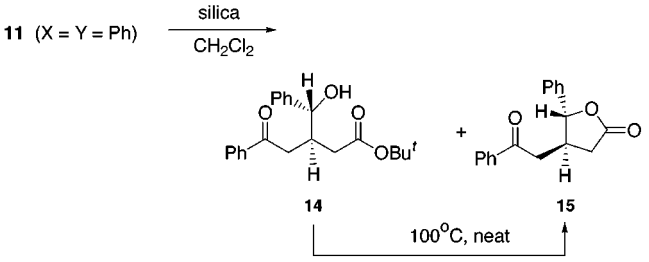
Scheme 2



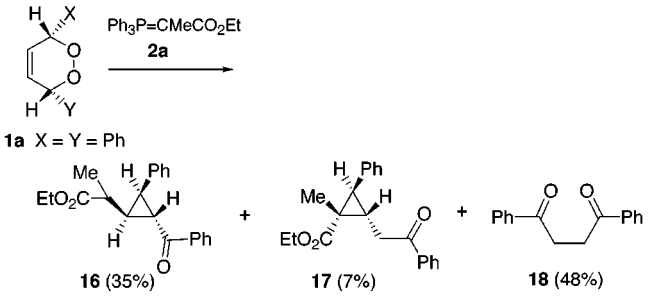
proposed mechanism indicates that cyclopropanes **7** and **8** should be formed with only a single deuterium being incorporated at position (H^4). Inspection of entry 3, Table 1, reveals this to be true. Finally, inspection of the data for entries 4 and 5 reveals that the overall cyclopropane product ratio (pathways a and b, Scheme 2) can be strongly influenced by the presence of deuterons. Thus, comparison of entries 2 and 4 indicates H−D exchange favors cyclopropanation pathway a over the second cyclopropanation pathway b. This observation is once again entirely consistent with our proposal, i.e., that factors such as the aforementioned conformational effects of bulky versus nonbulky R^1 substituents, or, in this case, the increased bond strength of the (O−D) bond within oxaphospholane **4**, would influence the likelihood of the nucleophilic carbon pole of the enolate **4** undergoing intramolecular S_N2 displacement of TPPO affording cyclopropane **5** versus enolate quenching. In addition, comparison of entries 4 and 5 indicates that the presence of H_2O also influences the overall cyclopropane ratio and reaction rates as compared to the situation when the reaction is conducted under anhydrous conditions. The presence of excess H_2O would be 'expected' to account for an increased likelihood of hydrolytic deprotonation of the proton attached to the oxaphospholane ring oxygen atom within **4**. This is also consistent with our previous observations that the second cyclopropanation pathway b is disfavored under concentrated conditions[4] due to an increased likelihood of removal of the proton attached to the oxaphospholane ring oxygen atom within **4** by excess ylide, thus leading to a situation where quenching of the enolate is disfavored/prohibited.

It was also of interest to note that the presence of nonanhydrous silica led to a number of hydrolysis products at the expense of cyclopropane formation. This result further supports the presence of the proposed intermediates **9** and **12**, Scheme 2. Thus, treatment of pure **11** (X = Y = Ph, R^1 = *t*-Bu) with silica (**11**/silica,

Scheme 3



Scheme 4



1:2 wt/wt) in CH_2Cl_2 for 30 min led to the formation of alcohol **14** and lactone **15** in a relative ratio of 26:74, Scheme 3. Interestingly, it was also observed by ^{1}H NMR that the presence of silica results in the spontaneous shifting of the **10**/**11** equilibrium toward almost entirely **11**. Isolation of pure **14** and heating to 100 °C in the neat form led exclusively to lactone **15**.

The trans relative stereochemistry within lactone **15** was fully established by single-crystal X-ray diffraction methods and is depicted in Figure 2. Mechanistically, the formation of trans **15** can be best rationalized by one of two scenarios, Scheme 2. Namely, (a) coordination of the silica to 1-2λ^5-oxaphospholane **9** followed by nucleophilic 'attack' by H_2O on the ring carbon atom attached to substituent (Y) with inversion, or (b) proton quenching of zwitterion **12** followed by nucleophilic H_2O 'attack' (with inversion) on the same carbon atom followed by TPPO expulsion.

Finally, we have previously highlighted that treatment of 1,2-dioxine **1a** (X = Y = Ph) with the bulky disubstituted ylide **2a** led to the formation of cyclopropane **16**,[4,6] which contains an extra stereogenic center within the side chain, along with a minor amount of cyclopropane **17** which must originate from the second cyclopropanation pathway b, Scheme 4. The remaining material being the isomeric 1,4-diketone **18** of the 1,2-dioxine.[4,6] Mechanistically, this observation is important in that methyl substitution of the ylide precludes the formation of **10** and **11**, thus indicating that their formation is not necessary for cyclopropane formation to occur via the second pathway. Furthermore, although it is conceivable that intramolecular quenching of the enolate of oxaphospholane **4** could lead directly to **10** without the intermediacy of oxaphospholane **9**, the formation of cyclopropane **17** precludes this possibility.

Optimization of Synthetic Potential. At this stage we felt it pertinent to further optimize the synthetic potential of these two cyclopropanation pathways in order to allow for the synthesis of cyclopropanes of type **5**, **7**, and **8** with minimum formation of mixtures. Additionally, while we have previously reported that the second cyclopropanation pathway b is favored over pathway a at subambient temperatures when bulky R^1 substituents are utilized,[4] we felt it would be convenient if protocols could be developed so that either pathway could be exploited at ambient temperature.

Scheme 5

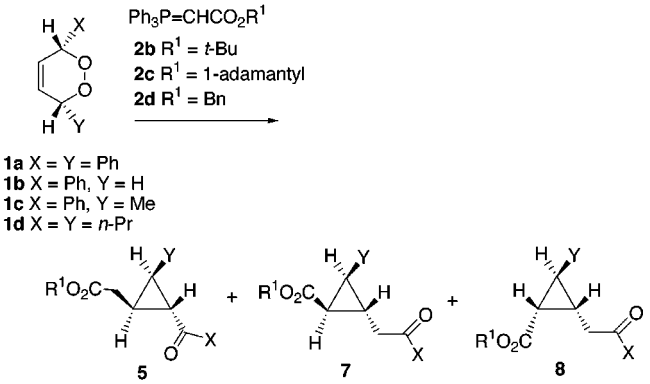


Table 2. Effect of Added LiBr on Cyclopropane outcome[a]

entry	1,2-dioxine	ylide (R^1)	additive[b]	products[c] (**5**:**7**:**8**%)
1[d]	**1a**	*t*-Bu	–	53:39:8
2[d]		*t*-Bu	LiBr (0.2 equiv)	0:50:4[f]
3[d]		*t*-Bu	LiBr (1 equiv)	0:60:5[f]
4[d,e]		*t*-Bu	–	0:91 (85):9
5[d,e]		1-Ad	–	17:70:13
6[d]		1-Ad	LiBr (0.1 equiv)	0:52 (45):4[f]
7[d,e]		1-Ad	–	26:66 (65):8
8	**1b**	*t*-Bu	–	84 (76): 15:1
9		*t*-Bu	LiBr (1 equiv)	11:80 (72):9
10		1-Ad	–	76:22:2
11		1-Ad	LiBr (1 equiv)	8:83 (58):9
12		Bn	–	100 (91)[g]:0:0
13		Bn	LiBr (0.2 equiv)	84:16:0
14		Bn	LiBr (1 equiv)	6:83 (68):11
15	**1c**	*t*-Bu	LiBr (1 equiv)	0:99 (78):1[h]
16[d]	**1d**	*t*-Bu	LiBr (1 equiv)	0:46 (40):4[f,h]

[a] All reactions performed under identical reaction volumes and concentrations (0.2 M) at ambient temperature in CH_2Cl_2 as solvent. Ylide (1.2 equiv) always employed with respect to 1,2-dioxine. See Experimental Section for typical procedure. [b] Added LiBr is always not totally soluble. [c] Ratio of products determined by ^{1}H NMR after cessation of reaction. All reactions resulted in 100% conversion of the starting material into cyclopropanes unless otherwise stated. Yields in brackets refer to isolated yields. [d] Performed in the presence of a catalytic amount (5 mol %) of Co(SALEN)$_2$. [e] The mixture was kept at −15 °C for 2 days after which time the mixture was allowed to attain ambient temperature. [f] Remaining material being unidentifiable products. Determined by ^{1}H NMR utilizing 1,4-dimethoxybenzene as internal standard. [g] Characterized in ref 4. [h] Cyclopropane **8** not characterized.

(a) Exploitation of Added LiBr To Favor Cyclopropanation Pathway b. Given that lithium ions are well-known to coordinate to enolate anions and influence their reactivity/selectivity we began analyzing the effect of added lithium bromide on these cyclopropanation pathways, the results of which are summarized in Table 2. For comparison, the results of identical experiments without added LiBr are also presented. Thus, treatment of 1,2-dioxine **1a** with the *tert*-butyl ester ylide **2b** or the 1-adamantyl ylide **2c** without added LiBr at ambient temperature resulted in approximately an equal mixture of cyclopropane **5**, originating from cyclopropanation pathway a, as compared to cyclopropanes (**7** and **8**), originating from pathway b, entries 1 and 5. Addition of LiBr to the same experiments resulted in a dramatic favoring of cyclopropane (**7** and **8**) over cyclopropane **5**; however, the actual overall cyclopropane yield dropped off dramatically, entries 2, 3, and 6. Importantly, while

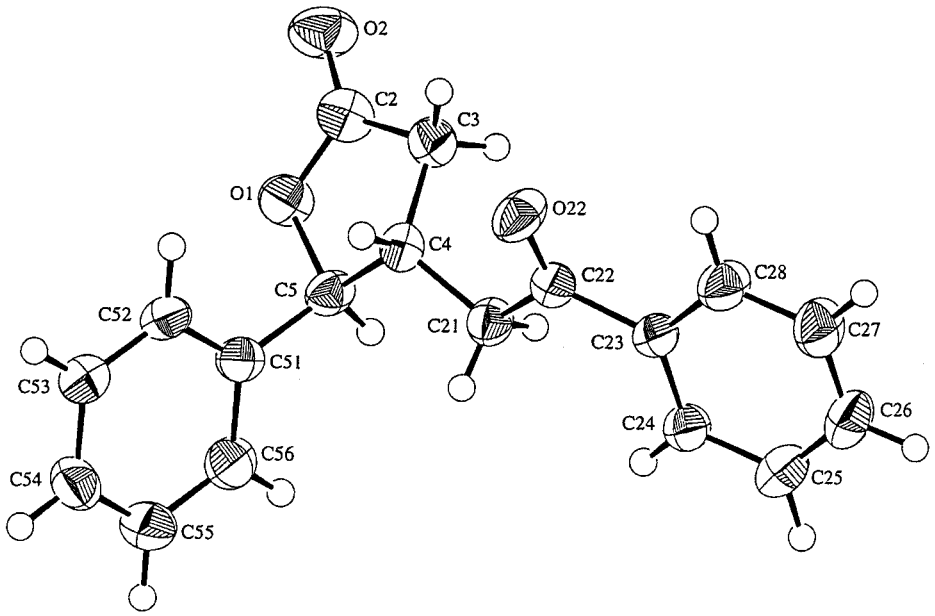


Figure 2. Molecular structure of lactone **15**.

this drop-off in yield was noticed when the 1,2-dioxine **1a** was utilized, no such drop-off was apparent when 1,2-dioxines (**1b**−**d**) were utilized, entries 9, 11, 13−16. Moreover, these dioxines also display a strong preference for formation of cyclopropanes (**7** and **8**) over cyclopropane **5** with added LiBr, compare entries 10 and 11 for example. Although added LiBr fails to allow us to control the selectivity between the two possible cyclopropanation pathways for 1,2-dioxine **1a**, we were still able to exploit lower temperatures to give rise to the situation where cyclopropanes (**7** and **8**) are favored over cyclopropane **5**, entries 4 and 5. In addition, it was also found that while nonbulky ylides such as **2d** (R^1 = Bn) only lead to cyclopropanes via pathway a (entry 12), the addition of LiBr could be exploited again, leading to favoring of (**7** and **8**) over **5**, entry 14. Thus, this observation further extends the scope of these cyclopropanation reactions, as cyclopropanes of type (**7** and **8**) can now be attained irrespective of whether the ylide utilized is bulky or nonbulky. The use of more than 1 equiv of LiBr fails to further improve the yield of cyclopropane **7**. The dramatic effect of lithium ions on reaction outcome is attributed to stabilization of enolate **4**, Scheme 2, resulting in the situation where intramolecular quenching of the enolate is favored over intramolecular cyclization to afford cyclopropanes **5**. It is also worth highlighting that added LiBr fails to lead to decomposition of the 1,2-dioxines **1** or their isomeric cis γ-hydroxy enones **3** and also failed to influence the decomposition of **11** into cyclopropanes **7** and **8**. This result further suggests that added LiBr must be influencing the reactivity of the oxaphospholane enolate **4**, and in the case of the poor cyclopropyl yield associated with the utilization of 1,2-dioxine **1a**, added LiBr may well be detrimental to cyclopropane yield when the substituent 'Y' is of the aryl type. Nevertheless, utilization of lower temperatures or dilute conditions can be exploited to overcome this.

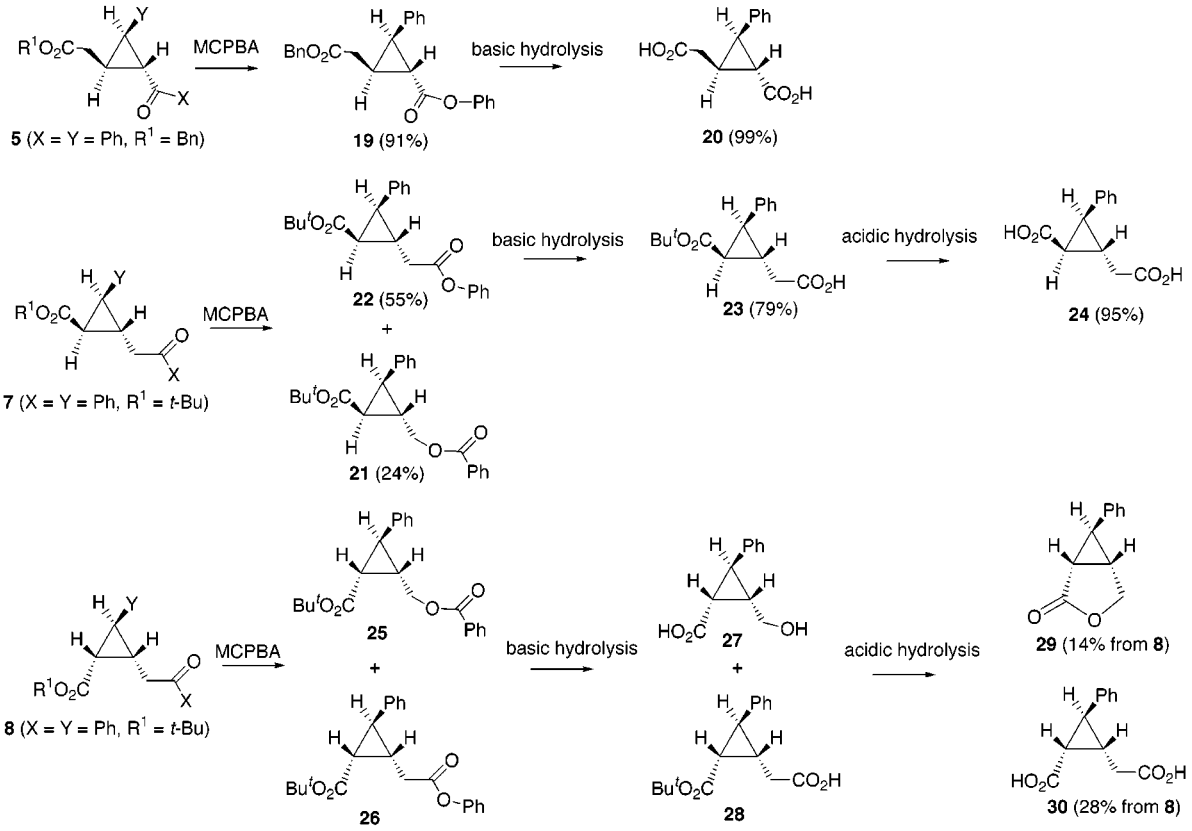
(b) Exploitation of Elevated Temperatures To Favor Stereoisomer 8 over 7. With protocols now developed for controlling the switching between the two cyclopropanation pathways, we next turned our attention to controlling the relative ratios of cyclopropane stereoisomers **7** and **8** derived from cyclopropanation pathway b. Inspection of the results collated in Table 3 reveals that conducting the experiment initially at −15 °C and then raising the temperature to ambient, favors the formation of stereoisomer **7** (X = Y = Ph and R^1 = *t*-Bu, entry 1) over **8**. However, conducting the same experiment at 60 °C or 100 °C results in an increased proportion of stereoisomer **8** at the expense of **7**, entries 2 and 3. In addition, allowing isolated **11** to collapse under similar conditions also leads to an increased proportion of stereoisomer **8** at elevated temperatures, entries 4 and 5. Most importantly was the observation that heating of **11** in the neat form at 170 °C or 205 °C led to a major preference for formation of stereoisomer **8**, entries 6 and 7. In addition, submitting an equal mixture of cyclopropanes **7** and **8** to the same experimental conditions failed to alter the cyclopropyl ratio indicating that no stereomutation of one isomer into the other was occurring at these elevated temperatures. Although the exact nature of why elevated temperatures favor cyclization through enolate **12b**, Scheme 2, is unclear at this stage, given that the cyclopropyl stereoisomers are easily separable by column chromatography this approach represents an

Table 3. Effect of Temperature on Collapse of 11[a]

entry	precursor	solvent	temp (°C)	reaction time[b]	products[c] (**5**:**7**:**8**%)
1[d]	**1a**	$CHCl_3$	−15 → 25	2 days + 2 days	0:91:9
2[d]	**1a**	$CHCl_3$	−15 → 60	2 days + 12 hrs	0:63:37
3[d]	**1a**	toluene	−15 → 100	2 days + 6 hrs	0:55:45
4	**11**	$CDCl_3$	25	2 days	0:86:14
5	**11**	$CDCl_3$	70	12 hrs	0:53:47
6[e]	**11**	neat	170	10 min	0:18:82
7[e]	**11**	neat	205	10 min	0:18:82

[a] All reactions performed under identical reaction volumes and concentrations (0.08 M) at the temperature specified. X = Y = Ph and R^1 = *t*-Bu for all entries. [b] Total reaction time necessary for conversion of starting material and any intermediates into cyclopropanes. [c] Ratio of products determined by ^{1}H NMR after cessation of reaction. All reactions resulted in 100% conversion of the starting material into cyclopropanes. [d] Reaction between 1,2-dioxine **1a** and ylide **2b** (1.2 equiv) conducted in the presence of a catalytic amount (5 mol %) of $Co(SALEN)_2$. The mixture was kept at −15 °C for 2 days after which time the complete mixture was added dropwise to an equal volume of solvent at the appropriate temperature [e] Finely powered **11** added to preheated flask.

Scheme 6



efficient method for synthesis of the cyclopropyl series **8**.

(c) Synthesis of Closely Related Cyclopropyl Stereoisomers. To demonstrate the potential of these new cyclopropanation reactions, we have exploited our optimized protocols to prepare three closely related cyclopropyl diacid stereoisomers, **20**, **24**, and **30**, Scheme 6. These diacids have close structural similarities to the metabotropic glutamate receptor (mGluR) agonist L-CCG-1.[13] Thus, Baeyer−Villiger oxidation of cyclopropane (**5**, X = Y = Ph, R^1 = *t*-Bu) obtained from the reaction between 1,2-dioxine **1a** and the benzyl ester ylide **2d** as described previously[4] resulted in the isolation of the diester **19** in 91% isolated yield. Subsequent hydrolysis afforded the diacid **20** in 99% yield. Alternatively, Baeyer−Villiger oxidation of cyclopropane **7** (X = Y = Ph, R^1 = *t*-Bu) obtained from the reaction between 1,2-dioxine **1a** and the *tert*-butyl ester ylide **2b** afforded cyclopropanes **21** and **22**. Isolation of the major cyclopropane isomer **22** followed by sequential hydrolysis of the ester groupings afforded the diacid **24** again in excellent yield. Finally, Baeyer−Villiger oxidation of cyclopropane **8** (X = Y = Ph, R^1 = *t*-Bu) obtained from the conditions set out in Table 3, entry 6, afforded the cyclopropyl diesters **25** and **26**. Sequential hydrolysis of the mixture of these diesters **25** and **26** under first basic conditions and then acidic conditions afforded the known cyclopropyl lactone **29**[14] from precursor **25** and the desired cyclopropyl diacid **30** from precursor **26**. Given the ease of formation of these three closely related cyclopropyl diacids, coupled with the fact that we have already shown that a range of substituents (X, Y = H, alkyl, aryl) can be accommodated for with this new methodology, Table 2, we conclude that this methodology has excellent potential for the synthesis of closely related cyclopropyl stereoisomers.

(13) Knöpfel, T.; Kuhn, R.; Allgeier, H. *J. Med. Chem.* **1995**, *38*, 1417.
(14) Shi, H.-J.; Wei, Q.; Wu, H.-J. *Youji Huaxue* **1997**, *17*, 76.

Conclusion

Through a combination of isolation, spectroscopic, temperature, and deuterium and additive effects studies, we have been able to propose a mechanism for cyclopropane formation resulting from the reaction of 1,2-dioxines **1** and bulky stabilized phosphorus ylides **2**. Key features of this second cyclopropanation pathway b, Scheme 2, include the ylide acting as a mild base inducing the ring opening of the 1,2-dioxines **1** to their isomeric cis γ-hydroxy enones **3**, followed by Michael addition of the ylide to the cis γ-hydroxy enones **3** and attachment of the electrophilic phosphorus pole of the ylide to the hydroxyl moiety affording the intermediate enolate of the 1-2λ^5-oxaphospholane **4**. Importantly, enolate quenching and oxaphospholane collapse results in an equilibrium mixture of **10** and **11** which have been fully characterized and their formation is primarily a result of the steric bulk of the stabilized ester ylide. This is in direct contrast to the situation when nonbulky ester ylides are utilized which results in a completely different cyclopropyl series.[4] These intermediates (**10**/**11**) then collapse further and result in formation of the observed closely related cyclopropyl stereoisomers **7** and **8**. Moreover, it has been found that the addition of LiBr to these reactions allows for controlling which of the two possible cyclopropanations presented pathways (a and b), Scheme 2, will be dominant. Finally, optimal protocols that demonstrate the potential of this new cyclopropanation methodology for the ready construction of closely related cyclopropyl stereoisomers have been presented.

Experimental Section

General Methods. Solvents were dried by appropriate methods wherever needed. All organic extracts were dried over anhydrous magnesium sulfate. Thin-layer chromatography (TLC) used aluminum sheets silica gel 60 F_{254} (40 × 80 mm) from Merck. Melting points were taken on a Reichert Thermovar Kofler apparatus and are uncorrected. Infrared spectra were recorded on an ATI Mattson Genesis Series FTIR spectrophotometer as Nujol mulls unless otherwise stated. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution on either a Varian Gemini 2000 (300 MHz) or Varian INOVA (600 MHz) instrument, TMS (0 ppm) and $CDCl_3$ (77.0 ppm) as internal standards unless otherwise specified. ABX spectra were analyzed by use of the effective Larmor frequencies method.[15] The correct analytical solution was then confirmed by spectral synthesis using VNMR 6.1B (Varian Inc., Palo Alto, CA). ^{31}P NMR chemical shifts referenced to 85% aqueous H_3PO_4 (external) in $CDCl_3$ with a negative shift indicating an upfield shift. All yields reported refer to isolated material judged to be homogeneous by TLC and NMR spectroscopy. The following materials were purchased from Aldrich and used without further purification: triphenylalkylidenephosphoranes (**2b** and **2d**), Co(SALEN)$_2$. The requisite 1,2-dioxines were prepared as described previously.[4] Prepared cyclopropanes with deuterium incorporation all had identical physical and chemical properties to those of their protio analogues.

***tert*-Butyl 2-(5-Hydroxy-2,5-diphenyltetrahydro-3-furanyl)-2-(1,1,1-triphenyl-λ^5-phosphanylidene)acetate (11).** To a mixture of 3,6-diphenyl-3,6-dihydro-1,2-dioxine **1a** (300 mg, 1.26 mmol) and *tert*-butyl 2-(triphenyl-λ^5-phosphanylidene) acetate **2b** (474 mg, 1.26 mmol) in acetonitrile (10 mL) was added Jacobsen's Co(SALEN)$_2$ complex (5 mg). The mixture was then stored in a freezer (−15 °C) for 2 days after which time was allowed to attain ambient temperature. After ca. 15 h the solvent was decanted and crystalline **11** triturated with a small portion of cold acetonitrile to afford **11** (124 mg, 16%). mp 156−158 °C (acetonitrile); IR 1593, 1378, 1014, 748, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.98 (s, 9H), 2.03 (dddd, J = 13.0, 8.4, 4.2 Hz, J_{H-P} = 13 Hz, 1H), 2.40 (dd, J = 13.0, 13.0 Hz, 1H), 2.63 (dd, J = 13.0, 4.2 Hz, 1H), 5.34 (d, J = 8.4 Hz, 1H), 7.07−7.59 (m, 23H), 7.75−7.77 (m, 2H), 9.56 (s, exch. D_2O, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 28.3, 40.4 (d, J_{C-P} = 122.0 Hz), 46.6 (d, J_{C-P} = 12.6 Hz), 49.4 (d, J_{C-P} = 5.4 Hz), 78.0, 82.4 (d, J_{C-P} = 5.4 Hz), 104.6, 125.3−133.4 (30 carbons), 142.5, 144.3, 169.9 (d, J_{C-P} = 12.6 Hz); ^{31}P NMR ($CDCl_3$, 121.4 MHz) δ 24.29; MS *m*/*z* (%): 615 (M^+, 0.1), 517 (60), 451 (28), 383 (81), 277 (78), 105 (100). Anal. Calcd for $C_{40}H_{39}O_4P$ (614.7): C, 78.16; H, 6.39. Found: C, 77.91; H, 6.54.

X-ray Structure of 11. Crystals of **11** suitable for X-ray crystallography were grown by slow (2 days) crystallization from acetonitrile as described above. $C_{40}H_{39}O_4P$, FW = 614.7, monoclinic, $P2_1/c$, a = 12.1865(3) Å, b = 15.1987(3) Å, c = 36.5583(8) Å, β = 98.8021(5)°, V = 6691.5(2) Å^3, Z = 8, D_{calc} = 1.220 g/cm^3, T = 123 K, μ = 1.22 cm^{-1}, $F(000)$ = 2608. Intensity data were measured for a colorless crystal (0.24 × 0.25 × 0.26 mm) on a Nonius Kappa CCD fitted with graphite monochromatized MoKα radiation, λ 0.71073 Å. A total of 57291 data (θ_{max} 27.8°) were measured, 16031 of which were unique and 8269 had $I \geq 2.5\sigma(I)$. The structure was solved by direct methods[16] and refined by a full-matrix least-squares procedure based on F.[17] Non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms were included in the model at their calculated positions. After the inclusion of a weighting scheme of the form $w = 1/[\sigma^2(F)]$, the refinement was continued until convergence when R = 0.043 and Rw = 0.045. The numbering scheme employed is shown in Figure 1 which was drawn with ORTEP at the 50% probability level.[18] Two independent molecules comprise the crystallographic asymmetric unit which differ from each other only trivially. Significant *intra*molecular hydrogen bonding is noted such that O(2a)−H···O(4a) is 1.72 Å, O(2a)···O(4a) is 2.667(2) Å, and the angle at H is 166°; the corresponding values for the second molecule are 1.71 Å, 2.668(2) Å, and 170°.

***tert*-Butyl 3-[Hydroxy(phenyl)methyl]-5-oxo-5-phenyl-2-(1,1,1-triphenyl-λ^5-phosphanylidene)pentanoate (10).** Although **10** can be adequately characterized by monitoring (^{1}H NMR) the reaction between the 1,2-dioxine **1a** and ylide **2b**, to avoid unnecessary complexity from overlaying resonances, the best approach was to characterize **10** formed from the equilibrium between **10** and **11**. Thus, **11** (20 mg) was dissolved in $CDCl_3$ (1.0 mL) and the mixture stored in a freezer (−15 °C) for 8 days after which time the mixture was analyzed. Ratio **10**:**11** (70:30). Data for **10**: IR ($CHCl_3$) 1672, 1596, 1438, 1104, 909 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.84 (s, 9H), 2.19 (ddd, J = 14.4, 3.0 Hz, J_{H-P} = 1.8 Hz, 1H), 2.48 (dddd, J = 12.0, 3.0, 1.8 Hz, J_{H-P} = 18.0 Hz, 1H), 4.53 (dd, J = 14.4, 12.0 Hz, 1H), 4.93 (brs, unresolved $^3J_{H-H}$ of 1.8 Hz and $^4J_{H-P}$ of 2.0 Hz, 1H), 6.66 (d, J = 7.2 Hz, 2H), 7.07−7.59 (m, 22H incl. OH), 7.83−7.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 28.2, 32.5 (d, J_{C-P} = 7.5 Hz), 43.1 (d, J_{C-P} = 12.0 Hz), 43.9 (d, J_{C-P} = 116 Hz), 77.8, 82.8 (d, J_{C-P} = 3.3 Hz), 125.3−138.0 (29 carbons), 144.4, 172.5, 203.3; ^{31}P NMR ($CDCl_3$, 121.4 MHz) δ 23.99.

Treatment of 11 with Silica. To a mixture of **11** (X, Y = Ph, R^1 = *t*-Bu) (100 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) at ambient temperature was added silica (200 mg) and the mixture stirred for 30 min after which time the silica was removed by filtration and the volatiles removed in vacuo. Subjecting the residue to column chromatography allowed for the isolation of alcohol **14** (14 mg, 24%) and lactone **15** (32 mg, 70%).

***tert*-Butyl 3-[Hydroxy(phenyl)methyl]-5-oxo-5-phenylpentanoate (14).** R_f 0.30 (4:1 hexane/ethyl acetate); IR (neat) 3480, 1724, 1681, 1598, 1581 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.39 (s, 9H), 2.38 (dd, J = 16.2, 4.4 Hz, 1H), 2.40 (dd, J = 16.2, 2.8 Hz, 1H), 2.91 (ddddd, J = 6.6, 6.6, 5.4, 4.4, 2.8 Hz, 1H), 3.05 (dd, J = 17.0, 6.6 Hz, 1H), 3.21 (dd, J = 17.0, 6.6 Hz, 1H), 3.23 (d, J = 5.4 Hz, exch.D_2O, 1H), 4.88 (dd, J = 5.4, 5.4 Hz, 1H), 7.24−7.27 (m, 1H), 7.30−7.37 (m, 4H), 7.42−7.45 (m, 2H), 7.53−7.56 (m, 1H), 7.91−7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 28.0, 35.0, 38.5, 39.3, 75.5, 80.9, 126.3, 127.5, 128.2, 128.4, 128.6, 133.2, 137.0, 142.8, 173.2, 199.8. The titled compound **14** was found to be relatively unstable undergoing cyclization to lactone **15** or decomposition.

***trans*-(±) 4-(2-Oxo-2-phenylethyl)-5-phenyltetrahydro-2-furanone (15).** R_f 0.15 (4:1 hexane/ethyl acetate); mp 102−103 °C (3:2 hexane/ethyl acetate); IR 1772, 1682, 1595, 1577 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.35 (dd, J = 16.8, 7.2 Hz, 1H), 3.00−3.09 (m, 2H), 3.15 (dd, J = 17.4, 8.4 Hz, 1H), 3.32 (dd, J = 17.4, 5.4 Hz, 1H), 5.22 (d, J = 6.6 Hz, 1H), 7.34−7.48 (m, 7H), 7.56−7.59 (m, 1H), 7.90−7.92 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 34.8, 40.0, 40.6, 85.5, 125.9, 127.9, 128.7, 128.8, 133.6, 136.3, 137.9, 176.0, 197.3; MS *m*/*z* (%): 280 (M^+, 6), 160 (50), 120 (82), 105 (100), 77 (52), 57 (15). Anal. Calcd for $C_{18}H_{16}O_3$ (280.3): C, 77.12; H, 5.75. Found: C, 76.95; H, 5.77.

X-ray Structure of *trans*-(±)-4-(2-Oxo-2-phenylethyl)-5-phenyltetrahydro-2-furanone (15). Crystals of **15** suitable for X-ray crystallography were grown by slow (2 days) crystallization from a combination of ethyl acetate in excess hexane. $C_{18}H_{16}O_3$, FW = 280.3, monoclinic, *P*bar1, a = 10.1551(9) Å, b = 17.267(1) Å, c = 9.6566(7) Å, α = 96.652(5)°, β = 117.933(6)°, γ = 93.107(7)°, V = 1474.5(2) Å^3, Z = 4, D_{calc} = 1.263 g/cm^3, T = 173 K, μ = 0.85 cm^{-1}, $F(000)$ = 592. Intensity data were measured for a colorless crystal (0.19 × 0.24 × 0.32 mm) a Rigaku AFC7R diffractometer fitted with graphite monochromatized Mo Kα radiation, λ 0.71073 Å. A total of 7153 data (θ_{max} 27.5°) were measured, 6773 of which were

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(17) *teXsan: Structure Analysis Software*; Molecular Structure Corporation: Texas, U.S.A, 1997.

(18) Johnson, C. K. *ORTEP, Report ORNL-5138*; Oak Ridge National Laboratory: TN, 1976.

unique and 3024 had $I \geq 3.0\sigma(I)$. The structure was solved by direct methods and refined as for **11**. After the inclusion of a weighting scheme of the form $w = 1/[\sigma^2(F) + 00002|F|^2]$, the refinement was continued until convergence when $R = 0.057$ and $Rw = 0.058$. The numbering scheme employed is shown in Figure 2 which was drawn with ORTEP at the 50% probability level.[18] Two independent molecules comprise the asymmetric unit, with only minor conformational differences between them.

***cis*-(±)-Ethyl 1-Methyl-2-(2-oxo-2-phenylethyl)-3-phenyl-1-cyclopropanecarboxylate (17).** A mixture of 3,6-diphenyl-3,6-dihydro-1,2-dioxine **1** (X = Y = Ph) (2.75 g, 11.6 mmol) was allowed to react with (carboethoxyethylidene)triphenylphosphorane **2a** (4.2 g, 11.6 mmol) in anhydrous dichloromethane (100 mL) under a nitrogen gas atmosphere at ambient temperature for 6 days. Removal of the volatiles in vacuo afforded the crude cyclopropanes **16**[4] and **17** along with diketone **18**. The title compound **17** (260 mg, 7%) was purified by first subjecting the crude material to column chromatography (5:1 hexane/ethyl acetate) and then again utilizing (19:1 benzene/ether) as the eluant. R_f 0.50 (19:1 benzene/ether); IR 1714, 1694, 1598, 1581 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.09 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.98 (ddd, J = 7.2, 7.2, 6.6 Hz, 1H), 2.87 (d, J = 7.2 Hz, 1H), 3.46 (dd, J = 18.3, 6.6 Hz, 1H), 3.53 (dd, J = 18.3, 7.2 Hz, 1H), 4.10−4.18 (m, 2H), 7.21−7.25 (m, 1H), 7.29−7.31 (m, 4H), 7.43−7.47 (m, 2H), 7.53−7.56 (m, 1H), 7.97−7.99 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.2, 16.0, 28.4, 29.5, 36.7, 37.0, 60.7, 126.7, 128.0, 128.2, 128.6, 129.4, 133.0, 136.9, 137.0, 174.1, 199.4; MS *m*/*z* (%): 323 (M^+, 41), 277 (50), 203 (10), 105 (100); HRMS of **17** ($C_{22}H_{30}O_3$) calcd, 323.1647; found, 323.1659.

Preparation of 1-Adamantyl 2-(1,1,1-triphenyl-λ^5-phosphanylidene) Acetate (2c). A solution of bromoacetic acid (6.35 g, 46 mmol), 1-adamantanol (3.5 g, 23 mmol), and *p*-toluenesulfonic acid (150 mg) were heated under reflux in benzene (60 mL) for 16 h with water being removed azeotropically. After cooling, the solution was washed with sodium bicarbonate (3 × 40 mL), and the aqueous washings were extracted with ether (30 mL). The combined organic extracts were then dried and the volatiles removed in vacuo to afford 1-adamantyl 2-bromoacetate (5.64 g, 90%) as a colorless oil.[19] A solution of 1-adamantyl 2-bromoacetate (5.64 g, 20 mmol) was added to triphenylphosphine (6.02 g, 23 mmol) in dry toluene (50 mL) and the mixture heated to 80 °C. After 16 h the precipitated white solid was collected by filtration and washed successively w) ith hexane (50 mL) and then ether (50 mL) and dried under an IR lamp. The salt was then dissolved in a minimal amount of methanol/water (1:1) and a solution of 1 N NaOH added dropwise with vigorous stirring until no more ylide precipitated. The precipitate was collected, washed with water (50 mL) and recrystallized from hexane to afford cream crystals of pure **2b** (6.4 g, 69%): mp = 145−148 °C; IR (Nujol) 2916, 1629, 1280, 1211, 1101, 1068; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.4−2.2 (m, 15H), 2.4−3.0 (brs, 1H), 7.36−7.68 (m, 15H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 30.7, 36.4, 41.0, 128.3 (d, J = 89.0 Hz), 128.4 (d, J = 12.0 Hz), 131.5 (d, J = 3.0 Hz), 132.8 (d, J = 9.8 Hz), 170.8; ^{31}P NMR ($CDCl_3$, 121.4 MHz) δ 17.48; MS (EI) *m*/*z* (%): 454 (M^+), 277 (100). Anal. Calcd for $C_{30}H_{31}O_2P$: C, 79.27; H, 6.87; Found: C, 78.82; H, 6.78.

Reaction of 1,2-Dioxines (1a−d) with Various Phosphoranes (2b−d). A Typical Procedure for Optimal Yield of Cyclopropanes 7. A mixture of 3,6-diphenyl-3,6-dihydro-1,2-dioxine **1a** (475 mg, 2.0 mmol) and anhydrous lithium bromide (174 mg, 2.0 mmol) was allowed to react with *tert*-butyl 2-(triphenyl-λ^5-phosphanylidene) acetate **2b** (903 mg, 2.4 mmol) in anhydrous dichloromethane (10 mL) under a nitrogen gas atmosphere at ambient temperature for 4 days, entry 3, Table 2. Removal of the volatiles in vacuo afforded the crude cyclopropane **7** (X = Y = Ph, R^1 = *t*-Bu) along with minor amounts (if any) of cyclopropanes **5** (X = Y = Ph, R^1 = *t*-Bu) and **8** (X = Y = Ph, R^1 = *t*-Bu). All examples collated in Table 2 were carried out under these standard conditions unless otherwise stated. Refer to Table 2 for reaction times, yields, and whether an added salt was utilized. Subsequent silica gel chromatography on the crude reaction mixture as specified for each cyclopropane below afforded the pure cyclopropanes.

***trans*-(±)-*tert*-Butyl 2-(2-Benzoyl-3-phenylcyclopropyl)acetate (5, X = Y = Ph, R^1 = *t*-Bu).** R_f 0.60 (4:1 hexane/ethyl acetate); mp 100−101 °C (heptane); IR 1733, 1656, 1596, 1577 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.34 (s, 9H), 2.08 (dd, J = 18.1, 10.3 Hz, 1H), 2.26−2.31 (m, 2H), 3.06 (dd, J = 4.9, 4.9 Hz, 1H), 3.13 (dd, J = 8.7, 4.9 Hz, 1H), 7.25−7.27 (m, 3H), 7.31−7.33 (m, 2H), 7.49−7.52 (m, 2H), 7.58−7.60 (m, 1H), 8.07−8.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.8, 27.9, 29.6, 33.5, 34.5, 80.6, 126.9, 128.1, 128.4, 128.6, 128.9, 132.9, 136.1, 137.8, 171.2, 198.5; MS *m*/*z* (%): 336 (M^+, 0.1), 281 (54), 221 (48), 105 (100), 77 (14), 57 (16). Anal. Calcd for $C_{22}H_{24}O_3$ (336.4): C, 78.54; H, 7.19. Found: C, 78.78; H, 6.90.

***trans*-(±)-*tert*-Butyl 2-(2-Oxo-2-phenylethyl)-3-phenylcyclopropane-1-carboxylate (7, X = Y = Ph, R^1 = *t*-Bu).** R_f 0.50 (4:1 hexane/ethyl acetate); mp 69−71 °C (heptane); IR 1712, 1693, 1596, 1581 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.14 (s, 9H), 1.90 (dd, J = 9.6, 4.8 Hz, 1H), 2.41-2.48 (m, 2H), 2.87 (dd, J = 16.8, 8.4 Hz, 1H), 3.43 (dd, J = 16.8, 4.8 Hz, 1H), 7.17−7.20 (m, 1H), 7.24−7.27 (m, 2H), 7.36−7.37 (m, 2H), 7.46−7.50 (m, 2H), 7.56−7.59 (m, 1H), 7.96−7.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.9, 27.7, 28.8, 32.3, 41.8, 80.3, 126.6, 127.9, 128.1, 128.7, 129.6, 133.2, 136.6, 136.7, 169.6, 198.5; MS *m*/*z* (%): 336 (M^+, 1), 281 (98), 263 (32), 105 (100), 77 (34). Anal. Calcd for $C_{22}H_{24}O_3$ (336.4): C, 78.54; H, 7.19. Found: C, 78.48; H, 6.96.

***cis*-(±)-*tert*-Butyl 2-(2-Oxo-2-phenylethyl)-3-phenylcyclopropane-1-carboxylate (8, X = Y = Ph, R^1 = *t*-Bu).** R_f 0.75 (4:1 hexane/ethyl acetate); mp 70−72 °C (heptane); IR 1712, 1689, 1598, 1581 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.40 (s, 9H), 2.06 (dddd, J = 9.6, 7.7, 6.6, 6.0 Hz, 1H), 2.45 (dd, J = 6.6, 5.4 Hz, 1H), 3.48 (dd, J = 18.2, 7.7 Hz, 1H), 3.52 (dd, J = 18.2, 6.0 Hz, 1H), 7.15−7.18 (m, 2H), 7.18−7.21 (m, 1H), 7.27−7.30 (m, 2H), 7.44−7.47 (m, 2H), 7.54−7.57 (m, 1H), 7.95−7.97 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 25.0, 28.1, 29.1, 30.9, 36.3, 80.8, 126.5, 128.0, 128.5, 128.6, 133.1, 137.0, 140.1, (one aromatic carbon masked), 171.3, 199.2; MS *m*/*z* (%): 336 (M^+, 6), 280 (15), 105 (100), 77(39), 57 (51). Anal. Calcd for $C_{22}H_{24}O_3$ (336.4): C, 78.54; H, 7.19. Found: C, 78.31; H, 7.01.

***trans*-(±)-1-Adamantyl 2-(2-Benzoyl-3-phenylcyclopropyl)acetate (5, X = Y = Ph, R^1 = 1-Ad).** R_f 0.13 (benzene); IR (Nujol): 2924, 1733, 1673, 1168, 1056 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.58 (brs, 6H), 1.97 (brs, 6H), 2.01−2.10 (m, 4H), 2.23−2.30 (m, 2H), 3.05 (dd, J = 4.5, 4.5 Hz, 1H), 3.14 (dd, J = 8.7, 5.1 Hz, 1H), 7.20−7.61 (m, 8H), 8.02−8.03 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9, 29.7, 30.7, 33.5, 34.6, 36.0, 41.1, 80.7, 126.8, 128.1, 128.3, 128.5, 128.9, 132.8, 136.1, 137.8, 170.9, 198.5; MS *m*/*z* (%): 414 (M^+, 15), 279 (80), 135 (100); HRMS of **5** (X = Y = Ph, R^1 = Ad) ($C_{28}H_{30}O_3$) calcd, 414.2194; found, 414.2185.

***trans*-(±)-1-Adamantyl 2-(2-Oxo-2-phenylethyl)-3-phenylcyclopropane-1-carboxylate (7, X = Y = Ph, R^1 = 1-Ad).** R_f 0.67 (4:1 hexane/ethyl acetate); mp = 102−104 °C (ether/pentane); IR 2923, 1695, 1690, 1593, 1273, 1212, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.52−1.54 (m, 6H); 1.73−1.77 (m, 6H), 1.89 (1H, dd, J = 9.0, 5.4 Hz), 2.01 (brs, 3H), 2.40−2.45 (m, 2H), 2.86 (dd, J = 17.4, 7.8 Hz, 1H), 3.44 (dd, J = 17.4, 4.2 Hz, 1H), 7.17−7.20 (m, 1H), 7.25−7.27 (m, 2H), 7.34−7.35 (m, 2H), 7.46−7.49 (m, 2H), 7.56−7.59 (m, 1H), 7.96−7.98 (m, 2H), ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.0, 28.9, 30.7, 32.4, 36.1, 41.0, 41.8, 80.4, 126.5, 127.8, 128.0, 128.6, 129.6, 133.1, 136.5, 136.7, 169.2, 198.3; MS *m*/*z* (%): 414 (M^+, 10), 135 (100). Anal. Calcd for $C_{28}H_{30}O_3$: C, 81.12; H, 7.29; Found: C, 81.26; H, 7.31.

***cis*-(±)-1-Adamantyl 2-(2-Oxo-2-phenylethyl)-3-phenylcyclopropane-1-carboxylate (8, X = Y = Ph, R^1 = 1-Ad).** R_f 0.23 (benzene); IR (neat): 2851, 1714, 1695, 1607, 1338, 1179, 1119, 1105 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.61−1.64 (m, 6H), 2.05−2.07 (m, 6H), 2.05 (dddd, J = 9.0, 7.7, 6.9, 6.0, 1H), 2.11 (brs, 3H), 2.15 (dd, J = 9.0, 5.4 Hz, 1H), 2.43

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(dd, J = 6.0, 5.4 Hz, 1H), 3.46 (dd, J = 18.0, 7.7 Hz, 1H), 3.51 (dd, J = 18.0, 6.9 Hz, 1H), 7.15−7.30 (m, 5H), 7.46−7.47 (m, 2H), 7.53−7.56 (m, 1H), 7.96−7.98 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.0, 29.2, 30.7, 30.9, 36.1, 36.2, 41.2, 80.9, 125.6, 126.3, 128.0, 128.3, 128.4, 128.5, 133.0, 140.0, 170.9, 199.0; MS m/z (%): 414 (M^+, 3), 279 (50), 262 (45), 135 (100); HRMS of **8** (X = Y = Ph, R^1 = 1-Ad) ($C_{22}H_{30}O_3$) calcd, 414.2194; found, 414.2182.

***trans*-(±)-*tert*-Butyl 2-(2-Benzoylcyclopropyl)acetate (5, X = Ph, Y= H, R^1 = *t*-Bu).** R_f 0.60 (4:1 hexane/ethyl acetate); mp 28−30 °C (heptane); IR (neat) 1730, 1668, 1599, 1579 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.98 (ddd, J = 8.1, 6.4, 4.1 Hz, 1H), 1.40 (s, 9H), 1.55 (ddd, J = 8.8, 4.8, 4.1 Hz, 1H), 1.85 (ddddd, J = 8.8, 7.8, 6.4, 6.4, 4.8 Hz, 1H), 2.24 (dd, J = 15.4, 7.8 Hz, 1H), 2.46 (dd, J = 15.4, 6.4 Hz, 1H), 2.58 (ddd, J = 8.1, 4.8, 4.8 Hz, 1H), 7.45−7.48 (m, 2H), 7.54−7.57 (m, 1H), 7.99−8.01 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 17.5, 22.0, 24.3, 28.0, 39.5, 80.7, 128.0, 128.4, 132.7, 137.9, 171.0, 199.3; MS m/z (%): 260 (M^+, 0.1), 205 (100), 187 (26), 105 (83), 77 (11), 57 (53). Anal. Calcd for $C_{16}H_2O_3$ (260.3): C, 73.82; H, 7.74. Found: C, 73.50; H, 7.13.

***trans*-(±)-*tert*-Butyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (7, X = Ph, Y= H, R^1 = *t*-Bu).** R_f 0.50 (4:1 hexane/ethyl acetate); mp 71−72 °C (heptane); IR 1720, 1683, 1595, 1578 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.75 (ddd, J = 8.3, 6.3, 4.5 Hz, 1H), 1.24 (ddd, J = 9.0, 4.5, 4.5 Hz, 1H), 1.38−1.46 (m, 10H), 1.76 (ddddd, J = 9.0, 7.5, 6.3, 6.1, 4.1 Hz, 1H), 2.82 (dd, J = 16.8, 7.5 Hz, 1H), 3.12 (dd, J = 16.8, 6.1 Hz, 1H), 7.45−7.47 (m, 2H), 7.55−7.58 (m, 1H), 7.92−7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 14.9, 17.4, 21.4, 28.3, 42.3, 80.5, 128.3, 128.9, 133.3, 136.9, 173.1, 198.6; MS m/z (%): 260 (M^+, 9), 204 (10), 187 (29), 105 (100), 77 (21), 57 (8). Anal. Calcd for $C_{16}H_2O_3$ (260.3): C, 73.82; H, 7.74. Found: C, 73.97; H, 7.58.

***cis*-(±)-*tert*-Butyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (5, X = Ph, Y= H, R^1 = *t*-Bu).** R_f 0.65 (4:1 hexane/ethyl acetate); mp 51−53 °C (heptane); IR 1714, 1687, 1594, 1577 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.93 (ddd, J = 7.2, 5.4, 4.8 Hz, 1H), 1.12 (ddd, J = 8.7, 8.1, 4.8 Hz, 1H), 1.38 (s, 9H), 1.67 (ddddd, J = 8.7, 8.7, 7.5, 7.2, 6.4 Hz, 1H), 1.82, (ddd, J = 8.7, 8.1, 5.4 Hz, 1H), 3.29 (dd, J = 18.0, 7.5 Hz, 1H), 3.34 (dd, J = 18.0, 6.4 Hz, 1H), 7.43−7.46 (m, 2H), 7.53−7.56 (m, 1H), 7.93−7.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.0, 15.9, 18.8, 28.1, 36.6, 80.4, 128.0, 128.5, 132.9, 137.0, 172.4, 199.5; MS m/z (%): 260 (M^+, 2), 205 (40), 187 (100), 105 (35), 77 (12), 57 (15). Anal. Calcd for $C_{16}H_2O_3$ (260.3): C, 73.82; H, 7.74. Found: C, 74.12; H, 7.83.

***trans*-(±)-1-Adamantyl 2-(2-Benzoylcyclopropyl)acetate (5, X = Ph, Y= H, R^1 = 1-Ad).** R_f 0.50 (2:98, ethyl acetate/benzene); IR (neat) 1727, 1668, 1598, 1450, 1402, 1223, 1180, 1056 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.98 (ddd, J = 8.0, 6.4, 4.0 Hz, 1H), 1.56 (ddd, J = 8.8, 4.8, 4.0 Hz, 1H), 1.61−1.63 (m, 6H), 1.84 (ddddd, J = 8.8, 7.8, 6.4, 6.4, 4.0, 1H), 2.03 (brs, 3H), 2.22 (dd, J = 15.3, 7.8 Hz, 1H), 2.46 (dd, J = 15.3, 6.4 Hz, 1H), 2.57 (ddd, J = 8.0, 4.8, 4.0 Hz, 1H), 7.45−7.46 (m, 2H), 7.55−7.56 (m, 1H), 7.99−8.00 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.5, 22.2, 24.4, 30.8, 36.1, 39.6, 41.3, 80.8, 128.0, 128.4, 132.7, 137.9, 170.8, 199.3; MS m/z (%): 339 (M^+ + H, 30), 135 (100). Anal. Calcd for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74; Found: C, 78.11; H, 7.86.

***trans*-(±)-1-Adamantyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (7, X = Ph, Y= H, R^1 = 1-Ad).** R_f 0.37 (2:98, ethyl acetate/benzene); mp = 101−102 °C (dichloromethane/hexane); IR 1714, 1685, 1268, 1085, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.76 (ddd, J = 8.6, 6.3, 4.5, 1H) 1.24 (ddd, J = 8.8, 4.6, 4.5, 1H), 1.42 (ddd, J = 8.6, 4.6, 4.3 Hz, 1H), 1.65 (brs, 6H), 1.76 (ddddd, J = 8.8, 7.2, 6.3, 6.0, 4.3, 1H), 2.11 (brs, 6H), 2.16 (brs, 3H), 2.80 (dd, J = 16.8, 7.2 Hz, 1H), 3.19 (dd, J = 16.8, 6.0 Hz, 1H), 7.40−7.60 (m, 3H), 7.94−7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.7, 17.2, 21.1, 30.7, 36.1, 41.3, 42.0, 80.4, 128.0, 128.6, 133.1, 136.5, 172.6, 198.4; MS m/z (%): 338 (M^+, 25), 203 (45), 135 (100). Anal. Calcd for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74; Found: C, 78.27; H, 7.83.

***cis*-(±)-1-Adamantyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (8, X = Ph, Y= H, R^1 = 1-Ad).** R_f 0.47 (2:98, ethyl acetate/benzene); IR 1715, 1687, 1394, 1178, 1058 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.91 (ddd, J = 7.0, 5.2, 4.6 Hz, 1H), 1.11 (ddd, J = 8.2, 8.1, 4.6 Hz, 1H), 1.60−1.63 (m, 6H), 1.65 (ddddd, J = 8.8, 8.2, 7.1, 7.0, 6.3, 1H), 1.76 (ddd, J = 8.8, 8.1, 5.2 Hz, 1H), 2.03−2.07 (m, 6H), 2.10 (brs, 3H), 3.28 (dd, J = 18.1, 7.1 Hz, 1H), 3.33 (dd, J = 18.1, 6.3 Hz, 1H), 7.41−7.47 (m, 2H), 7.50−7.58 (m, 1H), 7.93−7.97 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.0, 15.8, 18.7, 30.7, 36.1, 36.5, 41.3, 80.5, 128.0, 128.5, 132.9, 137.0, 172.2, 199.6; MS m/z (%): 339 (M^+ + H, 20), 135 (100); HRMS of **8** (X = Ph, Y= H, R^1 = 1-Ad) ($C_{22}H_{27}O_3$) calcd, 339.1960; found, 339.1953.

***trans*-(±)-Benzyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (7, X = Ph, Y = H, R^1 = Bn).** R_f 0.25 (1:9, ethyl acetate/hexane); mp = 82.5−83.5 °C (ether/pentane); IR 1724, 1683, 1267, 1025 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.86 (ddd, J = 8.8, 8.2, 4.5 1H), 1.37 (ddd, J = 8.7, 4.5, 4.5 Hz, 1H), 1.58 (ddd, J = 8.8, 4.5, 4.5 Hz), 1.89 (ddddd, J = 8.7, 8.2, 7.2, 6.6, 4.5, 1H), 2.89 (dd, J = 16.8, 7.2 Hz, 1H), 3.10 (dd, J = 16.8, 6.6 Hz), 5.12 and 5.14 (AB_q, J = 12.3 Hz, 2H), 7.3−7.6 (m, 6H), 7.9−7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.1, 17.8, 20.0, 41.9, 66.3, 128.0, 128.12, 128.14, 128.5, 128.6,133.2, 133.0, 136.5, 173.5, 198.0; MS m/z (%): 294 (M^+, 5) 188 (10), 105 (100). Anal. Calcd for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16; Found: C, 77.68; H, 6.08.

***cis*-(±)-Benzyl 2-(2-Oxo-2-phenylethyl)cyclopropane-1-carboxylate (8, X = Ph, Y = H, R^1 = Bn).** R_f 0.4 (benzene); IR (neat) 1727, 1687, 1451, 1401, 1162 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.03 (ddd, J = 7.2, 5.2, 4.9 Hz, 1H), 1.23 (ddd, J = 8.1, 8.1, 4.9 Hz, 1H), 1.77 (ddddd, J = 8.4, 8.1, 7.2, 7.0, 6.8, 1H), 1.95 (ddd, J = 8.4, 8.1, 5.2 Hz, 1H), 3.28 (dd, J = 20.0, 6.8 Hz, 1H), 3.34 (dd, J = 20.0, 7.0 Hz, 1H), 5.05 and 5.12 (AB_q, J = 12.0 Hz, 2H), 7.2−7.6 (m, 6H), 7.90−7.94 (2H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.77, 16.5, 17.7, 36.5, 66.3, 128.02, 128.08, 128.1, 128.4, 128.5, 132.9, 136.1, 136.8, 173.1, 199.2; MS m/z (%): 295 (M^+, 15), 188 (18), 105 (100), HRMS of **8** (X = Ph, Y = H, R^1 = Bn) $C_{19}H_{18}O_3$ (+H): calcd, 295.1334; found: 295.1344.

***trans*-(±)-*t*-Butyl 2-Methyl-3-(2-oxo-2-phenylethyl)-1-cyclopropanecarboxylate (7, X = Ph, Y= Me, R^1 = *t*-Bu).** R_f 0.25 (9:1 hexane/ethyl acetate); mp 47−49 °C (heptane); IR 1715, 1690, 1598, 1581 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.16 (ddq, J = 9.0, 6.0, 5.4 Hz, 1H), 1.23 (d, J = 6.0 Hz, 3H), 1.45 (s, 9H), 1.50 (dd, J = 9.0, 5.4 Hz, 1H), 1.62 (dddd, J = 7.8, 6.0, 5.4, 5.4 Hz, 1H), 2.75 (dd, J = 16.8, 7.8 Hz, 1H), 3.17 (dd, J = 16.8, 6.0 Hz, 1H), 7.45−7.47 (m, 2H), 7.55−7.57 (m, 1H), 7.91−7.93 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 11.7, 22.8, 22.8, 26.6, 28.2, 42.1, 80.3, 128.1, 128.7, 133.1, 136.8, 171.3, 198.8; MS m/z (%): 274 (M^+, 2), 219 (21), 201 (100), 105 (52), 77 (19), 57 (32). Anal. Calcd for $C_{17}H_{22}O_3$ (274.4): C, 74.42; H, 8.08. Found: C, 74.87; H, 8.02.

***trans*-(±)-*tert*-Butyl 2-(2-Oxopentyl)-3-propyl-1-cyclopropanecarboxylate (7, X = Y = Pr, R^1 = *t*-Bu).** R_f 0.4 (9:1, hexane/ethyl acetate); IR (neat) 1716, 1367, 1155 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.89 (t, J = 6.6 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 1.05 (m, 1H), 1.45−1.65 (m, 9H), 1.44 (s, 9H), 2.22 (dd, J = 16.2, 7.8 Hz, 1H), 2.41 (dd, J = 7.2, 7.2 Hz, 2H), 2.46 (dd, J = 16.2, 6.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.7, 13.7, 17.0, 21.9, 22.6, 26.0, 28.1, 28.7, 28.7, 44.1, 46.4, 80.2, 171.3, 209.5; MS m/z (%): 268 (M^+, 21), 211 (40), 196 (100); HRMS of **7** (X = Y = Pr, R^1 = *t*-Bu): calcd, $C_{16}H_{28}O_3$ (+H): 269.2117; found: 269.2113.

***cis*-(±)-*tert*-Butyl 2-(2-Oxopentyl)-3-propyl-1-cyclopropanecarboxylate (8, X = Y = Pr, R^1 = *t*-Bu).** R_f 0.6 (9:1, hexane/ethyl acetate); IR (neat) 1716, 1457, 1366, 1154 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.89 (t, J = 7.5 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H), 1.2−1.63 (m, 10H), 1.44 (s, 9H), 2.35 (t, J = 7.5 Hz, 2H), 2.66−2.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.7, 13.7, 17.2, 21.9, 23.0, 25.5, 27.2, 28.1, 34.9, 40.3, 44.5, 80.1, 172.3, 210.3; MS m/z (%): 269 (M^+ + H, 30), 213 (52), 195 (100); HRMS of **8** (X = Y = Pr, R^1 = *t*-Bu): calcd, $C_{16}H_{28}O_3$ (+H): 269.2117; found: 269.2113.

***trans*-(±)-Phenyl-2-[2-(benzyloxy)-2-oxoethyl]-3-phenylcyclopropane-1-carboxylate (19).** To a mixture of trans (**5**, X = Y = Ph, R^1 = Bn)[4] (0.35 g, 0.94 mmol) in CH_2Cl_2 (4 mL) was added *m*-CPBA (0.58 g, 0.94 mmol, 70%) and the

mixture stirred for two weeks after which time the insolubles were removed by filtration and a further portion of *m*-CPBA (0.58 g, 0.94 mmol, 70%) added. After a further two weeks, the mixture was again filtered, and the volatiles were removed in vacuo. The residue was subjected to column chromatography to afford the diester **19** (0.33 g, 91%). R_f 0.50 (19:1 benzene/ether); IR (neat) 1745, 1732, 1594, 1494 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.26−2.29 (m, 4H), 3.05 (dd, J = 8.9, 5.7 Hz, 1H), 5.09 and 5.11 (AB_q, J = 12.4 Hz, 2H), 7.08−7.11 (m, 2H), 7.20−7.40 (m, 13H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 24.8, 31.3, 32.8, 66.4, 121.5, 125.8, 127.1, 128.1, 128.2, 128.5, 128.5, 128.9, 134.9, 135.7, (one aromatic carbon masked), 150.7, 171.5; MS *m*/*z* (%): 386 (M^+, 1), 129 (6), 91 (100), 84 (11). Anal. Calcd for $C_{25}H_{22}O_4$ (386.5): C, 77.70; H, 5.74. Found: C, 77.54; H, 5.86.

***trans*-(±)-2-(Carboxymethyl)-3-phenylcyclopropane-1-carboxylic Acid (20).** To a mixture of the diester **19** (104 mg, 0.27 mmol) was added a mixture of H_2O and methanol (5 mL, 1:4 v/v) followed by the introduction of an aqueous KOH solution (2.0 mL, 2M) and the solution stirred for 15 h at ambient temperature. The mixture was then extracted with CH_2Cl_2 (2 × 5 mL) followed by acidification (concentrated HCl) of the aqueous phase. Further extraction with CH_2Cl_2 (3 × 5 mL), desiccation, and removal of the volatiles in vacuo afforded crude **20** which was further purified by recrystallization from dichloromethane/hexane (1:10) to afford pure diacid **20** (59 mg, 99%). mp 185−187 °C (dichloromethane/heptane); IR 1694, 1602, 1580 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.98 (dd, J = 16.8, 9.0 Hz, 1H), 2.07 (dd, J = 4.8, 4.8 Hz, 1H), 2.18 (dddd, J = 9.6, 9.0, 5.4, 4.8 Hz, 1H), 2.36 (dd, J = 16.8, 5.4 Hz, 1H), 2.96 (dd, J = 9.6, 4.8 Hz, 1H), 7.16−7.32 (m, 5H); ^{13}C NMR (8:1; $CDCl_3$/acetone-d_6, 75 MHz) δ 23.5, 23.9, 30.3, 31.8, 126.4, 127.9, 128.5, 135.1, 172.7, 174.0; MS *m*/*z* (%): 220 (M^+, 19), 202 (22), 174 (23), 129 (100), 115 (60), 91 (34); HRMS of **20** $C_{12}H_{12}O_4$ (+H): calcd, 221.0814; found: 221.0804.

Baeyer−Villiger Oxidation of (7, X = Y = Ph, R¹ = *t*-Bu). To a mixture of *trans*-**7** (X = Y = Ph, R^1 = *t*-Bu) (0.20 g, 0.60 mmol) in CH_2Cl_2 (3 mL) was added *m*-CPBA (0.22 g, 0.9 mmol, 70%) and the mixture stirred for 5 days after which time the insolubles were removed by filtration and the volatiles removed in vacuo. The residue was subjected to column chromatography to afford the diesters **21** (50 mg, 24%) and **22** (115 mg, 55%).

***trans*-(±)-[2-(*tert*-Butoxycarbonyl)-3-phenylcyclopropyl]methyl benzoate (21).** R_f 0.60 (4:1 hexane/ethyl acetate); mp 92−93 °C (heptane); IR 1712, 1601, 1583 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16 (s, 9H), 2.08 (dddd, J = 7.2, 6.8, 6.3, 5.3 Hz, 1H) 2.65 (dd, J = 9.8, 6.8 Hz, 1H), 4.32 (dd, J = 11.4, 7.2 Hz, 1H), 4.51 (dd, J = 11.4, 6.3 Hz, 1H), 7.20−7.28 (m, 5H), 7.43−7.49 (m, 2H), 7.55−7.60 (m, 1H), 8.06−8.09 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.9, 27.8, 27.9, 30.3, 66.0, 80.6, 126.8, 128.0, 128.4, 129.4, 129.8, 130.1, 133.0, 135.8, 166.5, 168.8; MS *m*/*z* (%): 352 (M^+, 2), 296 (100), 279 (94), 175 (49), 144 (23). Anal. Calcd for $C_{22}H_{24}O_4$ (352.4): C, 74.97; H, 6.86. Found: C, 74.87; H, 6.99.

***trans*-(±)-*tert*-Butyl-2-(2-oxo-2-phenoxyethyl)-3-phenylcyclopropane-1-carboxylate (22).** R_f 0.50 (4:1 hexane/ethyl acetate); mp 126−127 °C (heptane); IR 1759, 1713, 1589 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 9H), 1.96 (dd, J = 9.6, 4.8 Hz, 1H), 2.43−2.58 (m, 3H), 2.98 (dd, J = 15.3, 4.8 Hz, 1H), 7.08−7.12 (m, 2H), 7.19−7.29 (m, 4H), 7.33−7.41 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.1, 27.8, 29.0, 32.0, 37.6, 80.5, 121.5, 125.9, 126.8, 128.0, 129.5, 129.5, 136.1, 150.7, 169.2, 170.5; MS *m*/*z* (%): 352 (M^+, 0.1), 296 (78), 279 (100), 185 (38), 129 (49), 115 (76). Anal. Calcd for $C_{22}H_{24}O_4$ (352.4): C, 74.97; H, 6.86. Found: C, 74.66; H, 6.65.

***trans*-(±)-2-[2-(*tert*-Butoxycarbonyl)-3-phenylcyclopropyl]acetic acid (23).** To a mixture of the diester **22** (97 mg, 0.28 mmol) were added a mixture of H_2O and methanol (5 mL, 1:4 v/v) followed by the introduction of an aqueous KOH solution (2.0 mL, 2 M), and the solution was stirred for 15 h at ambient temperature. Water was then added (5 mL) and the mixture extracted with CH_2Cl_2 (2 × 5 mL) followed by acidification (concentrated HCl) of the aqueous phase. Further extraction with CH_2Cl_2 (3 × 5 mL), desiccation, and removal of the volatiles in vacuo afforded crude **23** which was further purified by recrystalization to afford pure mono-acid **23** (61 mg, 79%). mp 147−148 °C (1:8 dichloromethane/hexane); IR 1716, 1706, 1602 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.14 (s, 9H), 1.88 (dd, J = 9.5, 4.5 Hz, 1H), 2.27−2.37 (m, 2H), 2.46 (dd, J = 9.5, 6.0 Hz, 1H), 2.78 (dd, J = 19.8, 8.7 Hz, 1H), 7.19−7.33 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.6, 27.8, 29.0, 31.9, 37.1, 80.5, 126.7, 127.9, 129.4, 136.1, 169.3, 177.6; MS *m*/*z* (%): 276 (M^+, 1), 221 (48), 203 (40), 129 (59), 57 (100). Anal. Calcd for $C_{16}H_{20}O_4$ (276.3): C, 69.54; H, 7.29. Found: C, 69.50; H, 7.33.

***trans*-(±)-2-(Carboxymethyl)-3-phenylcyclopropane-1-carboxylic Acid (24).** To a mixture of the mono-ester **23** (50 mg, 0.18 mmol) in $CDCl_3$ (1 mL) was added trifluoroacetic acid (2 drops) and solution left standing for 15 h at ambient temperature. Removal of the volatiles in vacuo followed by recrystalization afforded pure diacid **24** (38 mg, 95%). mp 140−141 °C (1:10, dichloromethane/heptane); IR 1694, 1599, 1410 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.09 (dd, J = 9.6, 5.3 Hz, 1H), 2.47 (dddd, J = 7.5, 6.6, 6.6, 5.3 Hz, 1H), 2.60 (dd, J = 17.1, 7.5 Hz, 1H), 2.70 (dd, J = 9.6, 6.6 Hz, 1H), 2.75 (dd, J = 17.1, 6.6 Hz, 1H), 7.24−7.31 (m, 5H); ^{13}C NMR (8:1, $CDCl_3$/acetone-d_6, 75 MHz) δ 20.8, 27.2, 32.4, 36.6, 126.3, 127.6, 128.9, 135.6, 172.2, 173.6; MS *m*/*z* (%): 220 (M^+, 30), 174 (28), 129 (100), 115 (60), 91 (27). Anal. Calcd for $C_{12}H_{12}O_4$ (220.2): C, 65.45; H, 5.49. Found: C, 65.53; H, 5.50.

Baeyer−Villiger Oxidation of (8, X = Y = Ph, R¹ = *t*-Bu). To a mixture of *cis*-**8** (X = Y = Ph, R^1 = *t*-Bu) (0.3 g, 0.90 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (0.55 g, 2.25 mmol, 70%) and the mixture stirred for 11 days after which time the insolubles were removed by filtration and the volatiles removed in vacuo. The residue was then subjected to column chromatography (ethyl acetate/hexane, 1:4) to afford the inseparable diesters **25** and **26** in a relative ratio of 1:2. To these diesters was added a mixture of H_2O and methanol (5 mL, 1:4 v/v) followed by the introduction of an aqueous KOH solution (2.0 mL, 2 M) and the solution stirred for 15 h at ambient temperature. Water was then added (5 mL) and the mixture extracted with CH_2Cl_2 (2 × 5 mL) followed by acidification (concentrated HCl) of the aqueous phase. Further extraction with CH_2Cl_2 (3 × 5 mL), desiccation, and removal of the volatiles in vacuo afforded a crude mixture of the mono-acids **27** and **28** in a relative ratio of 1:2. These acids were then taken up in CH_2Cl_2 (3 mL) and treated with trifluoroacetic acid (1.5 mL) over 4 days at ambient temperature. A further portion of CH_2Cl_2 (2 mL) was then added, and the organics were washed with saturated bicarbonate (2 × 10 mL). Desiccation of the organic phase and removal of the volatiles in vacuo afforded the known lactone **29**[14] (22 mg, >99% purity). The combined aqueous washings were acidified to pH = 1 with concentrated HCl and then extracted with CH_2Cl_2 (3 × 10 mL) to afford the crude diacid **30** contaminated with some benzoic acid. Removal of the benzoic acid was achieved by sublimation (80 °C/0.01 mmHg) and the diacid further purified by recrystallization from heptane to afford pure **30** (48 mg, 24%). mp 127−129 °C (1:10, dichloromethane/heptane); IR 1712, 1687, 1602, 1580 cm^{-1}; ^1H NMR (acetone-d_6, 300 MHz) δ 2.14 (dddd, J = 9.0, 7.5, 6.9, 6.6 Hz, 1H), 2.27 (dd, J = 9.0, 5.0 Hz, 1H), 2.58 (dd, J = 6.6, 5.0 Hz, 1H), 2.93 (dd, J = 17.4, 7.5 Hz, 1H), 3.02 (dd, J = 17.4, 6.9 Hz, 1H), 7.32−7.49 (m, 5H); ^{13}C NMR (acetone-d_6, 75 MHz) δ 25.3, 26.9, 30.9, 31.0, 126.1, 126.2, 128.1, 139.9, 171.8, 172.5; MS *m*/*z* (%): 221 (M^+ + H, 42), 203 (100), 185 (22); HRMS of **30** $C_{12}H_{12}O_4$ (+H): calcd, 221.0814; found: 221.0814.

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